

**PATENT**Attorney Docket No. **AMBER-06311**

Attached hereto is a marked-up version of the changes made to the specification by the current amendment in conformity with 37 C.F.R 1.121(c)(1)(i-ii). The attached page is captioned, "Version With Markings To Show Changes Made".

**IN THE SPECIFICATION:**

Please replace the paragraph beginning at page 19, line 22 with the following rewritten paragraph:

- - Figure 11 provides examples of non-native amino acids with reporter properties, illustrates participation of a reporter in protein synthesis, and illustrates synthesis of a reporter.- -

Please replace the paragraph beginning at page 51, line 14 with the following rewritten paragraph:

- - The chemical synthesis of a reporter can be based on the linkage of a chemical moiety or a molecular component having reporter properties with a native amino acid residue. There are many fluorescent molecules which are sensitive to their environment and undergo a change in the wavelength of emitted light and yield of fluorescence. When these chemical moieties, coupled to amino acids, are incorporated into the synthesized protein, their environments are altered because of a difference between the bulk aqueous medium and the interior of a protein which can cause reduced accessibility to water, exposure to charged ionic groups, reduced mobility, and altered dielectric constant of the surrounding medium. Two such examples are shown in Figure 11.- -

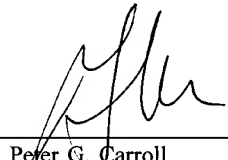
Please replace the paragraph beginning at page 52, line 14 with the following rewritten paragraph:

-- A second example of a reporter is a marker based on coumarin such as 6,7-(4', 5'-proline)coumarin. This compound can be chemically synthesized by coupling a fluorophore like coumarin with an amino-acid structural element in such a way that the fluorophore would alter its emission or absorption properties after forming a peptide linkage (Figure 11). For example, a proline ring containing secondary amino functions

**PATENT**Attorney Docket No. **AMBER-06311**

will participate in peptide bond formation similar to a normal primary amino group. Changes in fluorescence occur due to the co-planarity of the newly formed peptide group in relation to the existing fluorophore. This increases conjugation/delocalization due to the  $\pi$ -electrons of nitrogen-lone pair and carbonyl-group in the peptide bond. Synthesis of such compounds is based on coumarin synthesis using ethylacetoacetate (Figure 11). --

Respectfully submitted:

Dated: August 3, 2001  
\_\_\_\_\_  
Peter G. Carroll  
Registration No. 32,837

MEDLEN & CARROLL, LLP  
220 Montgomery Street, Suite 2200  
San Francisco, California 94104  
617.252.3353